REMARKS

Claims 1-15 and 18-28 are pending. Claims 9-15 and 18-28 have been withdrawn from consideration as being drawn to non-elected restriction groups. Claim 6 has been withdrawn from consideration as being drawn to a non-elected species. The withdrawn claims are not being canceled as Applicants understand that they are entitled to claims drawn to non-elected species upon allowance of a generic claim. Claims 16-17 were previously canceled. With this Amendment, claims 1 and 7 are being amended. Thus, after entry of this Amendment, Claims 1-5, 7 and 8 are under consideration. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail, below.

The Amendments of the Claims

Claim 1 has been amended to incorporate a limitation previously found in claim 7, and claim 7 has been amended to remove said limitation. Support for the amendments can be found in the as-filed specification, in at least the following places: page 15, second paragraph; page 17, second full paragraph; page 30, second full paragraph through the third full paragraph on page 31; and the last six lines of page 53; as well as original claim 7. No new matter is added by virtue of the amendments.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 2, 7 and 8 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kelly *et al.*, (WO 98/49146). Specifically, the Patent Office alleges that "Kelly, *et al.*, discloses a method for detecting inhibitors of CDK4 and identifies compounds that are more active against cancer cells than normal controls. (page 21 lines 8-26)." Applicants traverse the rejection.

Kelly, *et al.*, does not teach or suggest all the elements of the claimed methods. Kelly, *et al.*, relates to compounds that inhibit the kinase activity of CDK4. Kelly, *et al.*, does not teach or suggest methods for screening and identifying agents likely to disrupt other functions of critical normal gene products, such as non-kinase functions of CDK4. Throughout Kelly, *et al.*, the only activity of CDK4 assessed and found to be inhibited is its kinase activity (see page 17, lines 10-26). Moreover, page 6 of Kelly, *et al.*, defines the "inhibitory concentration" or "IC_{50}" dose of compound as "the drug concentration at 50% inhibition of kinase activity (μM)," and page 7 defines "CDK4 inhibitor" and "CDK4 inhibition" to refer to compounds inhibiting the kinase activity of CDK4. Furthermore, Kelly, *et al.*, define "CDK4 and "CDK4/A" to refer to the CDK4:cyclin D1 kinase holoenzyme (Kelly, *et al.*, page 6, lines 30-31), and Example 1 of Kelly, *et al.*, states that "the compounds of the invention were identified

and tested to determine their specific inhibitory activity against cyclin dependent kinases" and that the methods include three stages, wherein the third stage is "determining the CDK4 kinase inhibitory activity of selected, screened compounds." Thus, Kelly, *et al.*, does not teach or suggest methods for screening and identifying agents which disrupt a non-kinase function of a critical normal gene product such as CDK4.

For at least these reasons, Kelly, *et al.*, does not teach or suggest, and therefore does not anticipate, the methods recited in amended Claim 1. Therefore, Kelly, *et al.*, also cannot anticipate dependent Claims 2, 7 and 8. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 7 and 8 as being anticipated under 35 U.S.C. § 102(b) be withdrawn.

Rejection Under 35 U.S.C. § 103(a)

Claims 3-5 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kelly *et al.* in view of Theryte Limited (WO 99/42821). The Patent Office cites *Graham v. John Deere Co.*, an summarizes the factual inquiries applied for establishing a background for a determination of obviousness. Applicants traverse the rejection.

The Patent Office bears the initial burden of establishing a case of *prima facie* obviousness. *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1998); MPEP § 2142. If the Patent Office does not establish a *prima facie* case, the Applicants are under no obligation to submit evidence of non-obviousness, and the rejection must be withdrawn. *Id.*

To establish a proper *prima facie* case, three criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation that the modification or combination would be successful. Finally, the prior art reference (or references when combined) must teach all the limitations of the rejected claims. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based upon Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), *citing In re Dow*, 5 USPQ2d 1529 (Fed. Cir. 1988); MPEP § 2142.

At a minimum, the cited references, when combined, fail to teach or suggest each and every limitation of the rejected claims.

The Theryte reference is directed to methods for diagnosing cancer by testing for co-elevation of CDK1 and CDK4 protein levels. As described above, Kelly, *et al.*, teaches compounds that inhibit the

kinase activity of CDK4. As acknowledged by the Office, "Kelly et al does not disclose a cancer cell sample that consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6" (Office Action at page 4). The Office further cites the Theryte reference as disclosing that "CDK1 and CDK4 proteins are elevated in cancer cells (Figs. 3 and 4) and that the ration of CDK4 to CDK1 is approximately 1 (Fig. 5)." However, the references, even when combined, do not teach all the limitations of the rejected claims. Neither reference discloses inhibition of a non-kinase function of a critical normal gene product of the pending claims.

Furthermore, there is no suggestion or motivation, either in the references themselves or the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings to make the claimed combination. Even were there such suggestion or motivation, no reasonable expectation that the modification or combination would be successful is found in the prior art. In fact, as of Applicants' priority date, skilled artisans generally believed that critical normal gene products such as CDK4, acted through their kinase activity. As stated in the instant specification (at least at page 15, second paragraph; page 17, second full paragraph; page 30, second full paragraph through the third full paragraph on page 31; and the last six lines of page 53; as well as original claim 7), Applicants have unexpectedly found that the function of the CDK4 gene product required for successful division and continued cell survival of cancer cells, but not control cells, may be a function other than kinase activity.

Thus, the Office has failed to establish a *prima facie* case of obviousness, as the cited references do not teach or suggest all the limitations of pending claims. Applicants respectfully request that the rejection of claims 3-5 as being obvious under 35 U.S.C. § 103(a) in view of Kelly *et al.* combined with Theryte Limited (WO 99/42821) be withdrawn.

Conclusion

Claims 1-15 and 18-28 are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested.

No fees beyond the fee for a 1-month extension of time are believed to be due in connection with this Amendment. However, the Director is authorized to charge any additional fees that may required, or credit any overpayment, to Dechert LLP Deposit Account No. 50-2778 **(Order No. 376956-002US (368521))**.

Respectfully submitted,

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